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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,643	07/24/2006	Giovanni Monteleone	GIU-001	5446

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	**PAPER NUMBER**
1635	

NOTIFICATION DATE	DELIVERY MODE
06/11/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/551,643	MONTELEONE, GIOVANNI	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,20,21,23 and 25-29* is/are pending in the application.

4a) Of the above claim(s) *21,23 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,20 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/29/05,07/01/08,07/10/08,04/27/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 04/02/2009 is acknowledged. The traversal is on the ground(s) that groups I and II are sufficiently related for examination purposes and does not place a burden on the Patent Office. .

This is not found persuasive because as stated in the restriction requirement mailed 03/02/2009, the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. In the instant case the product antisense compound could be used in a materially different method such as *in situ* hybridization.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Application

Claims 10, 20, 21, 23, and 25-29 are pending. Claims 10, 20 and 26-29 are currently under examination. Claims 21, 23, 25 and non-elected subject matter are withdrawn as being drawn to a non-elected invention.

Information Disclosure Statement

The submission of the Information Disclosure Statements on 09/29/2005, 07/01/2008, 07/10/2008 and 04/27/2009 is in compliance with 37 CFR 19.7. The

information disclosure statements have been considered by the examiner and signed copies have been placed in the file.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10, 20 and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal et al. (US Patent No. 5,856,462 cited IDS filed 07/10/2008), Krieg et al. (cited on Applicant's IDS filed 09/29/2005) and Monia et al. (US Patent NO. 6,159,697 cited on IDS filed 07/01/2008).

The instant claims are drawn to an antisense oligonucleotide against Smad 7 comprising a sequence up to 21 nucleotides in length and consisting of SEQ ID No. 15, wherein X is cytosine, 5-methyl 2'-deoxycytidine or 5-methycytosine and Y is guanine and a pharmaceutical composition comprising said antisense and one or more pharmaceutically acceptable adjuvants and/or excipients.

Monia et al. teach Smad7 acts as an antagonist and interferes with the other Smad family members and interferes with signaling pathways involved in a diverse array of physiologic functions including cell proliferation and growth (see columns 1-2. Monia et al. teach antisense compounds targeted to the Smad7

gene and further teach methods of identifying efficient target sites and generating antisense oligonucleotides capable of inhibiting the expression of Smad 7. Monia et al. further teach said antisense compounds can contain modified sugar moieties such as 2'-O-methyl modifications as well as modified linkages (see columns 5-8 generally). Monia et al. do not specifically teach SEQ ID No. 15 nor teach incorporation of CpG motifs.

Agrawal et al. teach the use of modified oligonucleotides that are useful for studies of gene expression and the antisense therapeutic approach and teach modification of CpG motifs in antisense oligonucleotides to modulate gene expression with reduced splenomegaly and reduced depletion of platelets (see column 2). Agrawal et al. teach modified CpG dinucleotides comprising 5-methylcytosine and further teach chimeric or hybrid oligonucleotides wherein the oligonucleotide comprises regions containing DNA as well as RNA or 2'-O-substitued RNA. Agrawal et al. further teach modification of the CpG internucleoside linkages such as methylene phosphonate (see column 6). Agrawal et al. teach pharmaceutical compositions comprising pharmaceutically acceptable carriers (see column 5).

Krieg et al. teach oligonucleotides containing CpG dinucleotides trigger protective immune responses but this immune response is undesirable in antisense oligonucleotides. Krieg et al. teach the immune stimulation may be avoided in antisense oligonucleotides by the use of modified backbones and selective modifications of the cytosine nucleotides in any CpG dinucleotide.

Krieg et al. teach CpG containing oligonucleotides methylated at the 5 position of the cytosine lost their immune stimulatory activities (see page 109).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an antisense compound targeted to a Smad7 gene and to modify CpG motifs in the antisense compound targeted to Smad7 and to incorporate chemical modifications of nucleotides in the antisense compound to increase the stability of said compound.

One of ordinary skill in the art would have been capable of generating the claimed antisense compound as Monia et al. teach the cDNA sequence to said gene as well as steps to identify a specific target region and generate and test antisense compounds capable of inhibiting gene expression. One of ordinary skill in the art would have wanted to modify the antisense compounds that contain CG nucleotides as these nucleotides are well known in the art to cause unwanted immune stimulation in cells as taught by Krieg et al. One would have wanted to incorporate a 5 methylcytosine as taught by Agrawal et al. to decrease the unwanted immune stimulation. One would have wanted to further incorporate 2'-O substituted RNA along the antisense sequence, such as Monia et al. to increase the nuclease resistance and stability of the antisense oligonucleotide and it would have been a matter of routine optimization to incorporate such chemical modifications.

One of ordinary skill in the art would have a reasonable expectation of success at modifying the CpG dinucleotide motifs in an antisense oligonucleotide

given Agrawal et al. teach how to do so and teach reduced in vivo immune stimulation using modified CpG containing oligonucleotides.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center

supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Primary Examiner
Art Unit 1635